PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Poor Glycemic Control in Brazilian Patients with Type 2 Diabetes Attending the Public Healthcare System
AUTHORS	Viana, Luciana; Leitpo, Cristiane; Kramer, Caroline; Zucatti, Alessandra; Jezini, Deborah; Felicio, João; Valverde, Ana; Chacra, Antônio; Azevedo, Mirela; Gross, Jorge

VERSION 1 - REVIEW

REVIEWER	Dr. Ching Chiu Tufts University United Kingdom
REVIEW RETURNED	28-Jun-2013

GENERAL COMMENTS	This is a cross-sectional survey of blood glucose control in a cohort of 5,750 Brazilian type 2 diabetic patients attending the public healthcare system. The data is interesting and could be of clinical and public health significance. Reviewer has some suggestions below. 1. The American Diabetes Association recommends that the HbA1c should be below 53 mmol/mol (7.0%) for most patients. In page 7, line 2 of the manuscript, authors also stated that HbA1c <7% was found in only 26% of their patients. However, in Table 1 8% (the median for this cohort) was used as a cutoff point for the analysis. Reviewer thinks that using 7% as the cutoff is more clinically relevant and easy for comparison with other studies. 2. It is unclear that what confounders were adjusted in the Poisson regression (page 6, lines 18-28 and Table 1). Authors should clearly list them. 3. Figure 1 was not referred in the text and is redundant with Table 2. 4. Authors should double check their numbers throughout the manuscript. There are some errors, for example in Table 2: the percentage for over 8 years of education in Northeast should be 27% but not 34%.

REVIEWER	Professor John A McKnight University of Edinburgh Scotland UK No competing interests
REVIEW RETURNED	05-Jul-2013

THE STUDY	This is a nice study, well written and very clear. The main problem is

	selection of the population studied. This needs to be more clearly defined to enable interpretation of the results. The population of Brazil is very large, yet the authors describe results for around 5000 patients with diabetes, a very small proportion of the Brazilian diabetic population. Have they studied a group that is really representative? If this issue is clearly addressed I would be delighted to support publication of this work
RESULTS & CONCLUSIONS	It is curtical that this is described more clearly. I have called this a major revision rahter than minor to indicate how important this is.

VERSION 1 – AUTHOR RESPONSE

Answer to ProfessorChing Chiu
1) This is a cross-sectional survey of blood glucose control in a cohort of 5,750 Brazilian type 2 diabetic patients attending the public healthcare system. The data is interesting and could be of clinical and public health significance. Reviewer has some suggestions below.
Answer: Thank you for your comments. The answers are described below.

2) The American Diabetes Association recommends that the HbA1c should be below 53 mmol/mol (7.0%) for most patients. In page 7, line 2 of the manuscript, authors also stated that HbA1c <7% was found in only 26% of their patients. However, in Table 1 8% (the median for this cohort) was used as a cutoff point for the analysis. Reviewer thinks that using 7% as the cutoff is more clinically relevant and easy for comparison with other studies.
Answer: Thank you for this observation. We agree that usually the recommended target for HbA1c is below 7%. However, only 26% of your patients obtained HbA1c<7% and this aspect could have limited the statistical analyses. By using the median we obtained a more balanced distribution of the factors between the groups. Moreover, recently the American Diabetes Association considered that the goal of HbA1c should be individualized taking into account, among others, age, diabetes duration and presence of complications. So, in this context, we considered that the adopted cutoff value of HbA1c 8% adequate for our population with 61 ± 10 years old with diabetes duration of 11± 4 years. Nevertheless, we performed an analysis using the suggested cutoff and the results did not change substantially. A supplementary table using HbA1c≥7% was included in the manuscript. These comments were added to the conclusion section.

3) It is unclear that what confounders were adjusted in the Poisson regression (page 6, lines 18-28 and Table 1). Authors should clearly list them.
Answer: Poisson regression was adjusted for: age, diabetes, ethnicity, living with partner, working status, insulin use, SBMG, and geographic region. Adjustments for were included in the table 1.

4) Figure 1 was not referred in the text and is redundant with Table 2.
Answer: Thank you for your cautious revision. Figure 1 was deleted.

5) Authors should double check their numbers throughout the manuscript. There are some errors, for example in Table 2: the percentage for over 8 years of education in Northeast should be 27% but not 34%.
Answer: Thank you for careful review. We double checked the numbers of manuscript and we think they are now correct.

Answer to Professor John A McKnight
1) This is a nice study, well written and very clear. The main problem is selection of the population studied. This needs to be more clearly defined to enable interpretation of the results. The population of Brazil is very large, yet the authors describe results for around 5000 patients with diabetes, a very

small proportion of the Brazilian diabetic population. Have they studied a group that is really representative? If this issue is clearly addressed I would be delighted to support publication of this work

Answer: Thank you for your comments. This is a very important aspect and we would like to thank you for the opportunity to expand the rational of this study. The main objective of our study was to estimate the proportion of diabetic patients who needed to improve their metabolic control, which factors were associated with poor glycemic control, and to fundament government policies to implement strategies to improve diabetes care in the public healthcare system.

There are very few previous cohort and/or epidemiological studies in type 2 diabetes in Brazil. Some studies had included selected patients, such as those with some diabetic complications such as microalbuminuria (1,2) or microvascular or macrovascular complications (3), or evaluated specific ethnic groups (4). We identified only one study with a relatively unselected sample. That study assessed the prevalence of diabetes in the urban adult Brazilian population. It was a multicenter, cross-sectional survey in a random sample of individuals from nine large cities (5). Please find in the table below the main characteristics of the present study and the prevalence study.

Present study
Marlebi DA, Franco LJ
1992
n 5750 2294
Age (years) 61 ± 10 30-69
Female Sex 66.0% 64.7%
White ethnicity 44% 67.4%
DM duration (years) 11 ± 8.0 --
BMI (kg/m2) 28.0 ± 5.3 --
HbA1c (%) 8.6 ± 2.2 --

The main demographic characteristics of both sample of patients seems to be similar except by a higher prevalence of white subjects in the study of Malerby and Franco. However, the proportion of white subjects in our study reflects more the proportion of white individuals in Brazilian urban areas, 50% according the 2010 Census (Brazilian Institute of Geography and Statistics - IBGE, Instituto Brasileiro de Geografia e Estatística). Therefore we may consider that our sample is representative of diabetic patients in Brazil.

Moreover, we also calculated the sample size needed to estimate the prevalence of the adequate glycemic control based on the information that about 27% (range from 22% to 31%) (assumed rate) of type 2 diabetic patients in Brazil have an adequate glycemic control (data obtained from Social Security Health Minister). Considering an acceptable difference of 3% (half of the total width of the desired confidence interval of prevalence values of adequate glycemic control) the required number of patients was 1051 (alpha of 0•05; predicted subject loss of 20%; WinPepi, version 11.32 program). Besides this calculation, we included 5750 patients in order to be possible to evaluate each geographic region of Brazil. The sample size for each region was based, as close as possible, on the relative region distribution of population according to the Brazilian Institute of Geography and Statistics (IBGE, Instituto Brasileiro de Geografia e Estatística, Census 2000). We also considered that the data would be more reliable if they were collected from public health care centers that usually take care of at least three hundreds patients/month. So, we identified 14 centers located in the 12 most populous cities distributed along the five regions of Brazil. The table below shows the official distribution of Brazilian population in the five regions and the size of studied sample according each region.

Brazilian Regions Proportion of the population in each region considering total Brazilian population Patients included
n (%)
Total 100% 5750
North 7,9% 312 (5,4%)
Northest 28,0% 1906 (33,1%)

Southest 42,3% 2642 (45,9%)
South 14,5% 542 (9,4%)
Midwest 7,2% 348 (6,1%)

In conclusion, we may consider that the sample of diabetic patients included is representative of diabetes population living in urban centers. We can speculate that patients living in the rural areas of our country, who attend primary care units less equipped and with less trained health care personal, may have even a poorer diabetes control. Comments were added in the text in the Patients and Discussion sections.

References:

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3) Cardoso CR, Ferreira MT, Leite NC, Salles GF. Prognostic Impact of Aortic Stiffness in High-Risk Type 2 Diabetic Patients: The Rio de Janeiro Type 2 Diabetes Cohort Study. Diabetes Care 2013 Jul 22 [Epub ahead of print].
4) Gimeno SG, Ferreira SR, Franco LJ, Hirai AT, Matsumura L, Moisés RS. Prevalence and 7-year incidence of Type II diabetes mellitus in a Japanese-Brazilian population: an alarming public health problem. Diabetologia 2002 12:1635-8
5) Malerbi DA, Franco LJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in the urban Brazilian population aged 30-69 yr. The Brazilian Cooperative Group on the Study of Diabetes Prevalence. Diabetes Care 1992 11:1509-16.